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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/971,338	11/17/1997	SE-JIN LEE	GDF-1	4000

7590 06/24/2003

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EXAMINER
ALLEN, MARIANNE P

ART UNIT	PAPER NUMBER
1631	

DATE MAILED: 06/24/2003 #25

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action	Application No.	Applicant(s)	
	08/971,338	LEE, SE-JIN	
	Examiner	Art Unit	
	Marianne P. Allen	1631	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

PERIOD FOR REPLY [check either a) or b)]

a) ☐ The period for reply expires _____months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1.☒ A Notice of Appeal was filed on *21 March 2003*. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2.☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see Note below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____.

3.☐ Applicant's reply has overcome the following rejection(s): _____.

4.☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5.☐ The a)☐ affidavit, b)☐ exhibit, or c)☐ request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.

6.☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7.☒ For purposes of Appeal, the proposed amendment(s) a)☐ will not be entered or b)☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *none*.

Claim(s) objected to: *none*.

Claim(s) rejected: *4-10 and 22-33*.

Claim(s) withdrawn from consideration: _____.

8.☐ The proposed drawing correction filed on _____ is a)☐ approved or b)☐ disapproved by the Examiner.

9.☐ Note the attached Information Disclosure Statement(s)(PTO-1449) Paper No(s). _____.

10.☒ Other: *See attached comments and PTO-892*

Marianne P. Allen

Marianne P. Allen
Primary Examiner
Art Unit: 1631

EXAMINER'S COMMENTS

It is noted that the Appeal Brief was filed concurrently with this amendment after final rejection. Entry of this amendment results in cancellation of claims 34-35. As such, all rejections regarding claims 34-35 will be withdrawn. Addition of the limitations of claims 34-35 to claims 4 and 24 necessitates modifying the new matter rejection of record to correspond to independent claims 4 and 24 as well as dependent claims 5-7, 22, 25, and 28-30.

The modified ground of rejection is set forth below and will be set forth in the Examiner's Answer.

Claims 4-7, 22, 24-25, and 28-30 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 4 and 24 have been amended to include limitations to a protein encoded by a nucleic acid that hybridizes under conditions of 65 degrees Celsius and 1 M sodium chloride to DNA having the nucleotide sequence as defined in Figure 2 or Figure 11A or 11B and remains bound when subjected to washing at 68 degrees Celsius and 0.3 M sodium chloride/ 30 mM sodium citrate (2X SSC). As set forth in the prior Office actions, the specification does not disclose these limitations and as such the claims embrace new matter.

Appellant has previously pointed to page 10 and 17 of the specification for basis; however, the portion relied upon does not disclose the limitations as presently claimed.

The referenced portion of page 10 is reproduced below.

> identical to the sequence shown in **FIG. 2**. A "substantially identical" sequence is one the complement of which hybridizes to the sequence of **FIG. 2** at 68° C. and 1M NaCl and which remains bound when subjected to washing at 68° C. with 0.1×saline/sodium citrate (SSC) (note: 20×SSC=3M sodium chloride/0.3 M sodium citrate). The invention also

Note that this disclosure is with respect to the sequence of Figure 2 alone and not Figure 11A or 11B and that the hybridization is at 68 degrees Celsius and not 65 degrees Celsius.

The referenced portion of page 17 is reproduced below.

> For Southern analysis, DNA was electrophoresed on 1% agarose gels, transferred to nitrocellulose, and hybridized in 1M NaCl, 50 mM sodium phosphate, pH 6.5, 2 mM EDTA, 0.5% SDS, 10×Denhardt's at 65° C. The final wash was carried out in 2×SSC at 68° C.

Note that this disclosure is in the context of a particular experimental technique and is not associated with the what was intended by the prior disclosure of "substantially identical sequences." It is not disclosed with respect to hybridization of particular sequences in the absence of electrophoresis and transfer to nitrocellulose. It is not disclosed with hybridization to the particular sequences of Figure 2 or Figure 11A or 11B. Furthermore, the claims have no limitations corresponding to 50 mM sodium phosphate, pH 6.5, 2 mM EDTA, 0.5% SDS, and 10x Denhardt's which are clearly integral to this disclosure of hybridization at 65 degrees Celsius. There is nothing that ties these two separate portions of the disclosure together to convey to one of ordinary skill in the art that the invention now claimed was originally contemplated. It is further noted that the only Southern analysis performed in the specification in Example 3 on page 22 and in Figure 5, does not identify the sequence of the probe used but it appears that it must have been from mouse and not both mouse and human as encompassed by the claims in view of the limitations to Figures 2, 11A, and 11B.

The specification does not provide a limiting definition of the structural and functional requirements of the family of GDF-1 proteins for the reasons set forth in the prior Office actions; however, in view of the absence of support for the limitations now required by the amended claims as set forth above, this portion of the rejection is now moot.

In addition, appellant's brief presents arguments with respect to Akhurst et al. As set forth in the prior Office action, appellant has provided only the abstract to the examiner. Neither the abstract nor the full reference have been made of record by appellant. As such, the examiner provides the full reference for appellant and makes the reference of record. The reference discloses information about TGF-β1, TGF-β2, and TGF-β3 in mammalian embryogenesis. Akhurst et al. also discusses the wide variety of activities found in the larger TGF-β superfamily. Page 155 states, "As yet there is no definitive evidence that any of the TGFβs are endogenous regulators of mammalian embryonic processes." It is emphasized by the examiner that what is under discussion here is TGF-β itself and not the larger superfamily. Thus, this reference provides no evidence with respect to the proteins of the larger superfamily and their role in mammalian embryogenesis. Appellant is reminded that the protein disclosed to have the highest homology to GDF-1 was not TGF-β1, TGF-β2, or TGF-β3, but rather Vg-1 which is from amphibians and not mammals. The totality of Akhurst et al. fairly indicates that those of skill in the art at the time of the invention were experimenting and looking to see whether TGF-β1, TGF-β2, and TGF-β3 proteins were involved in mammalian embryogenesis and how. The conclusion and prospects section of the reference on pages 164-165 states that the evidence would suggest that each isoform of TGF-β (i.e. TGF-β1, TGF-β2, and TGF-β3) has a distinct function *in vivo*. The reference states, "To test this proposition, it is essential that more functional studies are carried out." This supports the examiner's position that further research would be required to reasonably determine or confirm any activity or involvement of GDF-1 in embryogenesis. Furthermore, the reference amply illustrates that embryogenesis is a highly diverse and complex process including skeletal development, hematopoiesis, vascularization, and so forth. (See pages 157-164.) This is also acknowledged by the specification as filed on page 2, lines 15-20. As such, a disclosure that

GDF-1 may be involved in embryogenesis cannot be considered to convey to those of ordinary skill in the art any specific or clear biological activity. It provides no direction or guidance as to which aspect or to a particular activity.

In addition, appellant's brief presents arguments with respect to Rankin et al. The reference was not made of record by appellant. As such, the examiner also includes this reference on the PTO-892. A copy was provided by appellant previously.

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